Influences on the Distribution of Blood Flow During Cardiac Tamponade in the Conscious Dog

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Cardiac tamponade is a spectrum ranging from pericardial effusions with minimal hemodynamic impairment to effusions causing circulatory collapse. In this study, we examined the roles played by the sympathetic nervous system and the renin-angiotensin system in controlling the distribution of blood flow in chronically instrumented conscious dogs during progressive cardiac tamponade. Fifty-one episodes of acute cardiac tamponade were induced to decompensation (decline in mean aortic blood pressure to 70% of the level present when the pericardium was free of fluid) in 6 dogs by intrapericardial infusion of warmed saline solution. Cardiac output (electromagnetic flow probe), intrapericardial pressure, aortic and right atrial blood pressures, and renal, coronary, and mesenteric artery blood flows (Doppler flow probes) were recorded during tamponade in the absence of blockade (control), during \( \alpha \)-adrenergic blockade (phenoxybenzamine), \( \beta \)-adrenergic blockade (propranolol), or angiotensin-converting enzyme blockade (captopril). Aortic and mesenteric artery blood flow decreased progressively during cardiac tamponade regardless of the presence or absence of blockade. Coronary artery blood flow did not significantly change during \( \alpha \)-adrenergic blockade, suggesting that the continuous decline observed during cardiac tamponade in the absence of blockade was at least in part mediated by \( \alpha \)-adrenergic mechanisms. Renal artery blood flow, in contrast, was well maintained in all situations, confirming the importance of autoregulation in this vascular bed during cardiac tamponade. (Circulation Research 1987;60:72-81)

Cardiac output and, ultimately, mean arterial blood pressure decrease during cardiac tamponade as increasing intrapericardial pressure limits diastolic filling of the heart.1,2 These alterations result in regional adjustments in organ perfusion and function.3-24 Sympathetic efferent nerve activity has been reported to increase during experimental cardiac tamponade,14 and the sympathetic nervous system has been shown to be involved in sustaining cardiac performance and augmenting venous return.16 The renin-angiotensin system is known to be important in the regulation of arterial blood pressure in other conditions that result in hemodynamic deterioration.17-19

Using radionuclide-labelled microspheres,20 previous investigators10-12 have studied regional blood flow during cardiac tamponade in closed-chest anesthetized acute canine preparations while the animals were artificially ventilated12 and after spontaneous respirations had resumed.10,11 Microspheres were injected at baseline (drained pericardium) and during cardiac tamponade when cardiac output had decreased by 50\%12 or arterial blood pressure had fallen 30-40 mm Hg.10,11 Blood flow to all organs declined significantly in these studies. Investigations using anesthetized open-chest dogs have shown regional myocardial blood flow during cardiac tamponade to be severely reduced.13 A 51\% decline in circumflex coronary artery blood flow (electromagnetic flow probe) has been described5 during cardiac tamponade in chronically instrumented awake dogs recovered from surgery at a time when cardiac output had fallen by 71\%.

With the exception of the present study, all past investigations have evaluated regional blood flow only at selected points in the progression of cardiac tamponade in anesthetized subjects or prior to complete recovery from surgery. In such preparations, the effects of anesthesia21-23 hormonal influences, organ metabolism, temperature, and acid-base status may have altered circulatory responses. In conscious dogs allowed less than 3 days to recover from surgery, we have consistently noted a continuous decline in arterial blood pressure during cardiac tamponade, whereas animals allowed to recover for at least 4 or 5 days maintained arterial blood pressure until late in cardiac tamponade when hemodynamic decompensation abruptly occurred.24 In this study, we examined the roles played by the sympathetic nervous system and the renin-angiotensin system in controlling the distribution of blood flow in chronically instrumented conscious dogs during progressive cardiac tamponade.

Materials and Methods

Six mongrel dogs weighing 24-30 kg were selected for study, screened for parasites, and fed a nutritious diet. Each animal was brought to the laboratory fol-
lowing an overnight fast, anesthetized (sodium pentobarbital, 25–30 mg/kg i.v. to effect), intubated, and ventilated by a volume respirator (Harvard Apparatus Company) using air enriched with oxygen (2–5 l/min). Using aseptic technique, a left flank incision was made with exposure of the renal (6 animals) and superior mesenteric (3 animals) arteries. Annular Doppler flow probes (manufactured in our laboratory) were placed around these vessels, taking special care to avoid damage to neural structures. We chose Doppler flow probes for measuring regional blood flow because they have an inherently stable zero (zero Doppler shift equals zero flow in the absence of electrical interference), eliminating the need for vascular occluders. The incisions were closed in layers, and the wires were tunneled subcutaneously to an area between the scapulae.

Four to five days later, a left thoracotomy in the fifth intercostal space was performed using aseptic technique. As before, the electrocardiogram and arterial blood gases were monitored throughout the procedure. A Tygon fluid-filled catheter (Tygon Micro bore Tubing, 0.050 inch i.d., 0.090 inch o.d.) was inserted into the left internal mammary vein, advanced to the right atrium, and secured. A second Tygon catheter was then passed through the right internal mammary artery and advanced into the proximal descending aorta with its position manually confirmed. Next, a catheter-tip micromanometer (PC-460, Millar Instruments) was inserted into the left internal mammary artery and advanced to the ascending aorta.

A 4–5 centimeter longitudinal incision was made in the pericardium overlying the pulmonary artery and left anterior descending coronary artery, and an electromagnetic flow probe was placed on the ascending aorta (Howell Instrument Company used with a Narcomatic electromagnetic flowmeter, Model RT-500, Narco Biosystems, Inc.). After careful exposure of the left anterior descending or circumflex coronary artery, a Doppler flow probe was placed around the vessel. Two fenestrated Tygon catheters were positioned in the pericardial space through separate incisions with their tips adjacent to the diaphragmatic surface of the left ventricle and were secured with purse-string sutures. The pericardium was carefully closed with a continuous locking suture, and a watertight seal was verified. A chest tube was placed through the seventh intercostal space, and all catheters and wires were passed individually through the chest wall and tunneled subcutaneously to an area between the scapulae. The ribs were approximated with umbilical tape, and the wound was closed in layers to provide an airtight seal. All intravascular catheters were flushed, filled with a heparin solution, and sealed. The chest was evacuated and the pericardial cavity was drained with continuous locking suture, and a watertight seal was achieved within 25 minutes using this protocol.

A maximum of 3 experiments were performed in a single day on a given animal with sufficient time allowed for recovery between episodes of cardiac tamponade. On the first day of study, 3 episodes of cardiac tamponade were performed on 3 animals in the absence of pharmacologic intervention (control). In the other 3 animals, 1 episode of cardiac tamponade under control conditions was followed by 2 episodes of cardiac tamponade during angiotensin-converting enzyme (ACE) blockade with captopril (1 mg/kg i.m. every 8 hours) was administered as needed for analgesia, and the animals received intramuscular injections of penicillin and streptomycin as a prophylactic measure.

Five days after surgery, the conscious animal was brought to the laboratory and allowed to stand comfortably in a sling. One of the pericardial catheters, the right atrial, and aortic catheters were attached directly to Statham P23Db pressure transducers (Statham Instrument Company) with the zero-pressure reference point one-third of the distance between the sternum and the spine. The Millar pressure transducer zero-pressure level was adjusted using the fluid-filled aortic catheter as a reference. The Doppler flow probes were used with a Hartley Doppler flowmeter. Baseline data were recorded after the pleural and pericardial cavities were drained of fluid, 5–10 ml normal saline had been replaced in the pericardial space, and a steady state had been achieved. When necessary, normal saline was infused intravenously so that the mean right atrial blood pressure in all animals was 0–4 mm Hg with the pericardium drained (baseline). Circumflex (or left anterior descending), renal, mesenteric, and aortic blood flows, intrapericardial pressure, and aortic and right atrial blood pressures were simultaneously recorded by an 8-channel FM tape recorder (Model D, A. R. Vetter Company) and an 8-channel Gould strip-chart recorder (Model 2800, Gould, Inc.). Cardiac tamponade was produced to decompensation by continuous intrapericardial infusion of warmed normal saline at a rate of 20 ml/min with a Masterflex infusion pump (Cole Parmer Instrument Company). Decompensated cardiac tamponade was defined as a decline in mean aortic blood pressure to 70% of the level present when the pericardium was empty and was achieved within 25 minutes using this protocol.

A maximum of 3 experiments were performed in a single day on a given animal with sufficient time allowed for recovery between episodes of cardiac tamponade. On the first day of study, 3 episodes of cardiac tamponade were performed on 3 animals in the absence of pharmacologic intervention (control). In the other 3 animals, 1 episode of cardiac tamponade under control conditions was followed by 2 episodes of cardiac tamponade during angiotensin-converting enzyme (ACE) blockade with captopril (1 mg/kg i.v., E.R. Squibb and Sons, Inc.). On the second day of study in all animals, 1 control episode of cardiac tamponade was followed by 2 episodes during β-adrenergic blockade (propranolol, 1 mg/kg i.v.). On the third day of study, 1 control episode of cardiac tamponade was followed by 2 episodes of cardiac tamponade during α-adrenergic blockade (phenoxybenzamine, 5 mg/kg i.v.). Forty-eight hours were allowed to elapse between each day of study in order to allow the effects of captopril and β-adrenergic blockade to dissipate. Completeness of ACE blockade with captopril was confirmed prior to data collection by noting the absence of a response to an intravenous injection of an amount of angiotensin 1, which had previously produced an increase in arterial blood pressure. Complete-
ness of β-adrenergic blockade was confirmed by the absence of a response to an intravenous bolus injection of an amount of isoproterenol that had consistently produced a slight decrease in arterial blood pressure and an increase in heart rate prior to blockade. Similarly, α-adrenergic blockade was confirmed by the absence of a phenylephrine-induced increase in arterial blood pressure. In all experiments, blockade was reconfirmed following completion of each episode of cardiac tamponade.

The positions of all catheters were noted after killing the animal. The circumflex (or left anterior descending), renal and mesenteric arteries, and the aorta all were removed with their flow probes in place. Calibration of the electromagnetic flow probe was performed by measuring timed collections of normal saline as it passed through the excised aorta with the flow probe in situ. In a similar fashion, the Doppler flow probes were calibrated by measuring timed collections of heparinized blood while recording the flowmeter output. All studies were conducted in a radio frequency shielded room to eliminate interference, and the relation between zero blood flow and zero Doppler shift was always checked following sacrifice.

All data were stored on analog magnetic tape and subsequently transferred to a digital computer (DEC LSI 11/23). Twenty-second data files were created at baseline and at each 2 mm Hg increment in intrapericardial pressure above baseline. Using sequential interactive programs, individual beats in the 20-second file were defined and mean pressures and flows were calculated. The time of each interval with respect to

FIGURE 1. Aortic blood pressure (mm Hg) during cardiac tamponade in the absence of blockade (control) and in the presence of β-adrenergic, α-adrenergic, or angiotensin-converting enzyme (ACE) blockade (mean ± SEM).

FIGURE 2. Blood flow during cardiac tamponade in the absence of blocking agents (control; Panel A) and in the presence of α-adrenergic (Panel B), β-adrenergic (Panel C), and angiotensin-converting enzyme (ACE; Panel D) blockade expressed as a percent of that present at baseline (mean ± SEM). See page 75.
B

C

D

Percent of baseline

Changes in IPP (mm Hg from baseline)
the onset of right ventricular diastolic collapse and decompensated cardiac tamponade were recorded, and a final file was created for statistical analysis.

Statistical Methods

Data were compared by repeated-measures analysis of variance using the absence (control) or presence of blockade (α-adrenergic, β-adrenergic, or ACE) as the grouping factor and the change in intrapericardial pressure as the repeated measure. In a similar fashion, a repeated-measures analysis of variance was performed with the vascular bed (renal, coronary, or mesenteric artery, or aorta) as the grouping factor. The group-by-within-subjects interaction was used to compare the overall slopes of the curves. Comparisons among means were made using the Waller-Duncan method for multiple comparisons. Linear contrasts were used to test for trends within a grouping factor, to evaluate changes from baseline, and to compare results across grouping factors.

Results

A total of 51 episodes of cardiac tamponade were studied in these chronically instrumented unanesthetized dogs: 23 control, 12 during β-adrenergic blockade, 10 during α-adrenergic blockade, and 6 under the influence of captopril. In Figure 1, the effect of cardiac tamponade on aortic blood pressure in the absence of blockade (control) and during α-adrenergic, β-adrenergic and ACE blockade is shown. Blood pressure in the control, β-adrenergic, and ACE blockade situations was maintained until late in cardiac tamponade, whereas during α-adrenergic blockade, blood pressure was poorly supported and fell rapidly (p<0.01).

Figure 2 illustrates the mean renal artery, coronary artery, mesenteric artery, and aortic blood flows during cardiac tamponade in the absence of blockade (control; Panel A) and during α-adrenergic (Panel B), β-adrenergic (Panel C), and ACE (Panel D) blockade. Blood flow is expressed as a percent of that present at baseline for each vessel. In the absence of blockade, there was no statistically significant change in renal artery blood flow during cardiac tamponade until intrapericardial pressure had increased to 16 and 20 mm Hg above baseline. In contrast, blood flow in the other vessels declined significantly (p<0.001) from baseline and behaved differently (p<0.001) from the renal bed. Decompensation during α-adrenergic blockade (Figure 2B) occurred with smaller changes in intrapericardial pressure than during control (Figure 2A), β-adrenergic (Figure 2C) or ACE (Figure 2D) blockade. Renal artery blood flow was significantly better maintained than coronary, mesenteric, and aortic blood flows during β-adrenergic or ACE blockade. Although coronary artery blood flow tended to be better preserved than aortic blood flow, this difference was not significant.

Figure 3 illustrates mean renal artery (Panel A), coronary artery (Panel B), mesenteric artery (Panel C), and aortic blood flows (Panel D) in the absence of blockade (control) and during α-adrenergic, β-adrenergic, and ACE blockade throughout cardiac tamponade. Renal artery blood flow did not change consistently from baseline except at the time of decompensated cardiac tamponade during α-adrenergic or ACE blockade. There were no significant differences in renal artery blood flow between cardiac tamponade in the absence of blockade and tamponade during α-adrenergic or ACE blockade. Renal artery blood flow during cardiac tamponade with β-adrenergic blockade, how-

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**Figure 3.** Renal (Panel A), coronary (Panel B), mesenteric (Panel C) artery, and aortic (Panel D) blood flows during cardiac tamponade in the absence of blockade (control) and in the presence of α-adrenergic, β-adrenergic, or angiotensin-converting enzyme (ACE) blockade (mean ± SEM). Panels A–C expressed as a percent of control baseline blood flow, Panel D as absolute flow. See page 77.
ever, differed from the control situation when intrapericardial pressure was 10, 12, and 14 mm Hg above the baseline value. Coronary artery blood flow decreased progressively during cardiac tamponade except under the influence of α-adrenergic blockade when it was variable and did not significantly change from its baseline. Aortic and mesenteric artery blood flow decreased progressively during cardiac tamponade, regardless of the presence or absence of blockade. Aortic blood flow during α-adrenergic blockade was initially greater ($p<0.001$) than with the other treatments but declined rapidly.

Figure 4 illustrates renal vascular resistance during cardiac tamponade in the presence of adrenergic or ACE blockade and in their absence. During cardiac tamponade, renal vascular resistance (defined as [arterial blood pressure − right atrial blood pressure]/renal artery blood flow) did not change from baseline except during β-adrenergic blockade at 12, 16, and 18 mm Hg increase in intrapericardial pressure. α-Adrenergic blockade resulted in a consistently decreased renal vascular resistance compared to that found during tamponade in the absence of blockade. Figure 5 illustrates the effect of β-adrenergic blockade on heart rate and stroke volume during cardiac tamponade. Heart rate was lower at baseline during β-adrenergic blockade than it was in the absence of blockade and did not increase normally. Stroke volume (calculated as aortic blood flow measured beyond the origin of the coronary arteries divided by heart rate) was consistently higher in the presence of β-adrenergic blockade.

**Discussion**

Cardiac tamponade may be viewed as a spectrum ranging from pericardial effusions with minimal hemodynamic impairment, which may be asymptomatic, to effusions with severe cardiac compression and circulatory collapse. In this study, the use of Doppler and electromagnetic flow probes has allowed the continuous measurement of regional blood flow during the entire progression of acute cardiac tamponade in a conscious animal completely recovered from surgery.

Renal artery blood flow was vigorously maintained during cardiac tamponade to the point of hemodynamic decompensation regardless of pharmacologic mediation and despite a dramatic decline in cardiac output. At the same time, renal vascular resistance was largely unaffected by adrenergic or ACE blockade, confirming the importance of autoregulation in maintaining renal blood flow during cardiac tamponade. It appears that the kidney receives the blood flow it requires despite a decrease in cardiac output and arterial blood pressure. Our findings are not in agreement with those of previous investigators. Millard et al found a 25% decrease in blood flow to the renal cortex during cardiac tamponade when cardiac output had decreased by 50% in closed-chest anesthetized dogs. Likewise, Martins et al and Gascho et al found arterial blood flow to the kidney decreased by 42–46% when cardiac tamponade had decreased arterial blood pressure by 30–40 mm Hg in acute, closed-chest, spontaneously breathing, anesthetized dogs. These divergent results were recorded despite the fact that the endpoints selected by previous investigators all occurred earlier than our “endpoint” of decompensation, defined as a decline in mean arterial blood pressure to 70% of baseline. In our study, decompensation corresponded to an approximate 66% decline in cardiac output (Figure 3D). The contrasting effects of cardiac tamponade on renal artery blood flow in conscious vs. anesthetized dogs are consistent with those observed by Vatner during hemorrhage. Anesthetized animals were less able to defend against the stress of a declining cardiac output in each situation and experienced a fall in arterial blood pressure and a failure to autoregulate renal blood flow. Clearly, conscious animals that have recovered from surgery respond to the stress of cardiac tamponade differently from acute preparations.

Cardiac tamponade is known to be a potent antinatriuretic force, yet we have found renal artery blood flow...
flow to be extremely well preserved in this conscious model. Osborn and Lawton, using an anesthetized canine model of cardiac tamponade, found urinary sodium excretion to be reduced, renin secretion rate and efferent renal nerve activity to be increased, and aortic blood pressure, renal artery blood flow, and glomerular filtration rate to be unchanged early in tamponade when intrapericardial pressure was 5 mm Hg. This effect of cardiac tamponade on urinary sodium excretion was prevented by renal denervation or bilateral cervical vagotomy, leading them to suggest that the response was neurally mediated and dependent on afferent sensory information from pericardial, cardiac, or splanchnic receptors. At 10 mm Hg, intrapericardial pressure, aortic blood pressure, and glomerular filtration rate decreased. The decline in urine sodium excretion was prevented by renal denervation but was unaffected by bilateral cervical vagotomy, suggesting that arterial baroreceptor unloading contributes to the production of antinatriuresis during advanced cardiac tamponade.

Coronary artery blood flow during control conditions and during β-adrenergic or ACE blockade does decline progressively \((p \leq 0.01)\) during cardiac tamponade (Figure 3B) but to a lesser extent than does aortic blood flow (Figure 2A, C, and D). The marked decline in coronary artery blood flow during cardiac tamponade in the absence of blockade in this study is similar to the 30–70% decline from baseline coronary artery blood flow shown by many other investigators. Coronary artery blood flow during α-adrenergic blockade was variable and showed no significant change from baseline. Although decompensated cardiac tamponade occurred earlier during α-adrenergic blockade, this finding does suggest that α-adrenergic tone may influence the decrease in coronary artery blood flow seen in the absence of α-blockade. The mechanism of this decrease in coronary artery blood flow during cardiac tamponade, however, remains to be clarified. It has been suggested that the decline in coronary artery blood flow is appropriate to the reduced needs of the heart during cardiac tamponade, but others have reported that the myocardium may be ischemic, thus contributing to hemodynamic collapse. We have found no evidence that myocardial ischemia contributes to the hemodynamic changes associated with acute cardiac tamponade in unanesthetized animal preparations.

With the dramatic decline in aortic blood flow, the smaller decline in coronary blood flow, and the preser-
viation of renal artery blood flow, other less vital vascular beds must receive less than their normal proportion of cardiac output. Mesenteric artery blood flow was measured as an example of a region that probably would not be favored. Our results are consistent with this analysis.

Figure 1 illustrates that aortic blood pressure was well maintained in the absence of blocking agents (control) but declined late in cardiac tamponade during \( \beta \)-adrenergic blockade. Cardiac output in both groups was essentially the same (Figure 3D). Figures 5A and 5B demonstrate that heart rate was higher at baseline and increased to a greater extent during cardiac tamponade in the control situation than during \( \beta \)-adrenergic blockade, whereas stroke volume was consistently lower. If we make the reasonable assumption that the left ventricular ejection fraction during cardiac tamponade in the control situation was greater than, or equal to, that found with \( \beta \)-adrenergic blockade, we may conclude that the left ventricular end diastolic volume at any intrapericardial pressure must be greater during \( \beta \)-adrenergic blockade than in its absence, and the increased stroke volume we observed in this situation must depend on the Frank-Starling mechanism. This deduction is consistent with observations in anesthetized animals showing left ventricular end systolic diameter to be greater during cardiac tamponade with \( \beta \)-adrenergic blockade than during tamponade before blockade.

The regional blood flow responses during cardiac tamponade in this study are similar to those observed by Vatner in conscious dogs and primates during hemorrhage. Blood flow to the mesenteric and iliac beds showed a greater reduction than coronary blood flow, whereas renal blood flow rose above control levels during moderate hypotensive hemorrhage.

Despite a decline in aortic blood flow to approximately 34% of its baseline level in the absence of blockade (Figure 2A), aortic blood pressure was remarkably stable (Figure 1) under control conditions but began to fall late in cardiac tamponade during both \( \beta \)-adrenergic and ACE blockade. During \( \alpha \)-adrenergic blockade, mean aortic blood pressure was significantly lower and fell rapidly during cardiac tamponade. \( \alpha \)-Adrenergic mechanisms thus play a central role in adjusting to the stress of cardiac tamponade.

In conclusion, during acute progressive cardiac tamponade in a conscious euvoicemic canine model recovered from surgery, \( \alpha \)-adrenergic mechanisms played a major role and the renin-angiotensin system a lesser role in the overall regulation of aortic blood pressure and flow. Regionally, the continuous decline in coronary artery blood flow was less severe than the fall in cardiac output, and the regulation of this vascular bed during cardiac tamponade was influenced by \( \alpha \)-adrenergic mechanisms. Renal artery blood flow during acute progressive cardiac tamponade was intensely autoregulated independent of adrenergic and renin-angiotensin mechanisms. Certainly the ability to maintain regional blood flow during cardiac tamponade in these healthy, euvoicemic conscious dogs was limited, and it could be speculated that in situations of coexisting factors, such as coronary artery disease, ventricular dysfunction, and renal disease, these mechanisms may not be effective.

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References

18. Reid IA, Brooks VL, Rudolph CD, Keil LC: Analysis of the
actions of angiotensin on the central nervous system of conscious dogs. Am J Physiol 1982;243:R82-R91


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